

Cancer Incidence and Mortality Among Finnish Asbestos Sprayers and in Asbestosis and Silicosis Patients

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Cohorts of Finnish asbestos sprayers and of asbestosis and silicosis patients were followed for cancer with the aid of the Finnish Cancer Registry in the period 1967-1994. Compared with the cancer incidence of the total Finnish population, asbestos sprayers had an increased risk for total cancer (standardized incidence ratio [SIR] 6.7, 95% confidence interval [95% CI] 4.2-10); lung cancer (SIR 17, 95% CI 8.2-31); and mesothelioma (SIR 263, 95% CI 85-614). The SIR of the asbestosis patients was 3.7 (95% CI 2.8-5.0) for all sites, 10 (95% CI 6.9-14) for lung cancer, and 65 (95% CI 13-188) for mesothelioma. The silicosis patients also had significantly high SIR values for all sites (1.5, 95% CI 1.0-2.1) and lung cancer (2.7, 95% CI 1.5-4.5). The values for the SIR and the standardized mortality ratio for all sites and lung cancer were very similar, and therefore it seems that both are reliable indicators of the occurrence of occupational cancer. It was concluded that pneumoconioses patients and asbestos-exposed workers have a markedly elevated risk for cancer. Asbestos-induced occupational cancers are not only diseases of the elderly, since the relative risk is high also for middle-aged people. Am. J. Ind. Med. 31:693-698, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: asbestos; asbestosis; silicosis; neoplasms; occupation; mortality; cohort study; record linkage

INTRODUCTION

Asbestos is a well known carcinogen, and asbestosis patients and persons exposed to crocidolite asbestos have the greatest risk [IARC, 1987; Stayner et al., 1996]. There is also increasing evidence for a higher risk of lung cancer in association with silicosis [Partanen et al., 1995; Smith et al., 1995; Steenland et al., 1996]. Exposure to asbestos and silica

occurs in numerous occupations. Finnish asbestosis patients include sprayers heavily exposed to crocidolite, asbestos quarry workers exposed to anthophyllite, asbestos cement factory workers whose primary exposure is to chrysotile, and insulation workers who usually have a mixed exposure to different types of asbestos. Typical silicosis patients are stone workers, mine and quarry workers, foundry workers, construction workers, and glass, clay, and pottery workers.

In this study we have evaluated the cancer morbidity of Finnish asbestos sprayers and of asbestosis and silicosis patients.

SUBJECTS AND METHODS

Study Population

Asbestos spraying was performed in Finland in 1955-1976 and was thereafter prohibited. Approximately 200 workers had worked in the trade for some time in

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TABLE I. Cohort Members by Demographic Variables: 1967–1994

	Asbestos sprayers (n)	Asbestosis patients (n)	Silicosis patients (n)
Gender			
Male	129	118	163
Female	4	10	7
Smoking			
Nonsmokers	10 (17%)	23 (18%)	30 (18%)
Smokers	29 (48%)	45 (35%)	57 (34%)
Ex-smokers	21 (35%)	60 (47%)	83 (49%)
	60 (100%)	128 (100%)	170 (100%)
No data	73	—	—
Occupation			
Insulation workers		53	
Asbestos quarry workers		24	
Asbestos cement factory workers		24	
Asbestos sprayers	133	14	
Other asbestos workers		12	
Stone, quarry, and mine workers			44
Foundry workers			72
Glass, clay, and pottery workers			17
Construction workers			20
Other workers exposed to silica (e.g., grinders, sand blowers)			17

1955–1976, some of them for only a few months. In a later follow-up of this cohort, through the Finnish Registry of Work-Related Diseases (August, 1994), there were 33 (26%) cases of asbestosis and 13 (10%) cases of benign pleural disease in the cohort.

In 1987, 134 asbestos sprayers were identified through employee registers and other sources. They constituted the asbestos-sprayer cohort of the present study (Table I). All the living members of the cohort were invited to a health examination in 1987. Sixty of them participated, and data on smoking habits and duration of asbestos exposure were available only for them. The mean duration of asbestos exposure among the 60 examined asbestos sprayers was three years (range 0.2–13).

The asbestosis and silicosis cohorts (Table I) were formed in 1977–1985 from patients who visited the Finnish Institute of Occupational Health for a periodic health examination because of previously diagnosed asbestosis or silicosis, or who were diagnosed at the Institute as having asbestosis or silicosis. The average profusion of the small opacities in the beginning of the follow-up was ILO 1/1 for the asbestosis patients and ILO 2/1 for the silicosis patients. Smoking habits and exposure data were recorded during

TABLE II. Number of Men in Follow-up and Number of Person-Years at Risk in 1967–1994, by Cohort^a and Age^b

Age category	Asbestos sprayers		Asbestosis patients		Silicosis patients	
	N	P-years	N	P-years	N	P-years
All	129	2,632	118	1,903	163	1,782
<30 years	78	474	—	—	—	—
30–44 years	46	1,452	18	78	10	62
45–59 years	5	675	60	556	89	617
60–74 years	—	32	39	551	64	986
75+ years	—	—	1	72	—	117

^aFourteen men belonged to both the asbestos sprayer and asbestosis cohorts, and one man belonged to both the silicosis and asbestosis cohorts.

^bAge at the beginning of the follow-up.

clinical examinations at the Institute. The mean duration of exposure was 21 (range 4–40) years for the asbestosis patients and 24 (range 9–43) years for the silicosis patients. Fourteen men belonged both to the asbestos sprayer and asbestosis cohorts, and one man was included in both the silicosis and asbestosis cohorts.

There were 129 asbestos sprayers, 118 asbestosis patients, and 163 silicosis patients, all male, under follow-up in the cohort. The numbers of person-years were 2600, 1300, and 1800, and the mean lengths of follow-up 20, 11, and 11 years, respectively.

Follow-up

The identification of the persons and the follow-up for death and emigration for the years 1967–1994 was done through the Population Register Center, using as the key the unique identification number given to everyone residing in Finland since 1 January, 1967. Three men from the cohort of asbestos sprayers had to be excluded because of missing identification data.

Follow-up for cancer was done automatically through the files of the Finnish Cancer Registry; follow-up for causes of death was done through Statistics Finland. The follow-up started on 1 January, 1967; or on January first of the year following the year of first employment as an asbestos sprayer, or January first of the year following the first periodic health examination since 1977 for the asbestosis and silicosis patients. The calculation of person-years ended at emigration or death, or on 31 December, 1994, whichever occurred first (Table II).

The number of incident cancer cases and the number of deaths among the cohort members, as well as the person-years at risk, were counted by five-year age groups, separately for three calendar periods (1967–1975, 1976–1984, and 1985–1994). Further division was made by follow-up

TABLE III. Observed Numbers of Cancer (Obs) and the Standardized Incidence Ratios (SIR) with the 95% Confidence Intervals (95% CI) for the Men in 1967–1994, by Cohort

Primary site	Asbestos sprayers			Asbestosis patients			Silicosis patients		
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
All sites	22	6.7	4.2–10	47	3.7	2.8–5.0	31	1.5	1.0–2.1
Mesothelioma	5	263	85–614	3	65	13–188	—	0.1 ^a	0–50
Lung, bronchus	10	17	8.2–31	33	10	6.9–14	15	2.7	1.5–4.5
Other sites	7	2.6	1.0–5.4	11	1.2	0.6–2.1	16	1.0	0.6–1.7

^aExpected number.

since first employment or the date of diagnosis of asbestosis or silicosis, and by smoking category and occupation (Table I).

The expected numbers of deaths were based on national sex-specific, period-specific, and cause-specific mortality rates. The expected numbers of cases for total cancer and specific cancer types were calculated by multiplying the number of person-years in each age group by the corresponding average cancer incidence for cancer in Finland during the period of observation. The a priori-selected specific cancer types included the cancer sites with known or suspected exceptional risk among asbestos-exposed persons in earlier studies [IARC, 1987; Partanen et al., 1994], as well as the other common cancer types, so that the information on cancer would be complete for the study cohorts.

Statistical Methods

In the calculation of the standardized incidence ratio (SIR) and standardized mortality ratio (SMR), the observed number of cases was divided by the expected number. The statistical significance was tested by the Mantel-Haenszel chi-square test on the presumption that the number of observed cases followed a Poisson distribution. The term "statistically significant" refers to $P < 0.05$ or a 95% confidence interval (95% CI) that does not include 1.00. Since no smoking-specific reference data were available for cancer incidence, the smoking-specific risks of cancer were calculated using expected numbers from the general Finnish population.

RESULTS

Cancer Incidence

During the follow-up period, 22 cases of cancer were found among the male asbestos sprayers (Table III). The expected number was 3.3, and the SIR was significantly high at 6.7. There were five cases of mesothelioma (SIR 263) and ten cases of lung cancer (SIR 17). Two of the five

mesotheliomas were peritoneal. The risk of lung cancer was elevated for all the separately analyzed histological types: adenocarcinoma (SIR 28, 95% CI 5.7–81), small cell carcinoma (SIR 17, 95% CI 2.0–60), and squamous cell carcinoma (SIR 11, 95% CI 1.3–39). The combined SIR of cancers other than mesothelioma and lung cancer was 2.6 (95% CI 1.0–5.4, $P < 0.05$).

Among the male asbestosis patients there were 47 cases of cancer versus 13 expected (SIR 3.7). There were three cases of mesothelioma (SIR 65) and 33 cases of lung cancer (SIR 10). The excess of lung cancer risk was significant for all the main histological types: adenocarcinoma (SIR 14, 95% CI 5.3–31), small cell carcinoma (SIR 11, 95% CI 4.0–24), and squamous cell carcinoma (SIR 6.1, 95% CI 2.4–13). The mesotheliomas among the asbestosis patients were all pleural. The incidence of cancers other than mesothelioma and lung cancer was not increased (Table III).

The male silicosis patients had 31 cases of cancer versus 21 expected (SIR 1.5, 95% CI 1.0–2.1, $P < 0.05$). There were no mesotheliomas (expected number 0.1); however, the incidence of cancer of the lung (SIR 2.7) was significantly high, and that of cancer of the urinary bladder (SIR 2.4, 95% CI 0.5–6.9) was increased, although nonsignificantly. Among silicosis patients there were five squamous, two adeno, and two small cell lung carcinomas: for five cases there was no histology available. The number of specific histologies was too low for further analyses.

About one-half of the lung cancers were attributed to a given lobe: among these, about two-thirds were situated in the lower lobes both among the asbestos sprayers and the asbestosis patients combined (14/21), and among the silicosis patients (5/8). Smoking was strongly associated with the incidence of lung cancer (Table IV). In the nonsmoking category there were no cancer cases. The relative risk of lung cancer was highest among the middle-aged asbestos-exposed men (Table V).

There were only four female asbestos sprayers, ten female asbestosis patients, and seven female silicosis

TABLE IV. Observed Numbers of Lung Cancer (Obs) and the Standardized Incidence Ratios (SIR) with the 95% Confidence Intervals (95% CI) for the Men in 1967–1994, by Cohort and Smoking Category

Smoking category	Asbestos sprayers			Asbestosis patients			Silicosis patients		
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
Nonsmokers	—	0.1 ^a	0.0–57	—	0.6 ^a	0.0–6.2	—	1.1 ^a	0.0–3.5
Ex-smokers	1	8.8	0.2–49	14	6.8	3.7–11	6	2.0	0.7–4.4
Smokers	2	13	1.5–46	19	30	18–47	9	6.1	2.8–11
Smoking unknown	7	28	11–58						

^aExpected number.**TABLE V.** Observed Numbers of Lung Cancer (Obs) and the Standardized Incidence Ratios (SIR) with the 95% Confidence Intervals (95% CI) for the Men in 1967–1994, by Cohort and Age

Age category	Asbestos sprayers			Asbestosis patients			Silicosis patients		
	Obs	SIR	95% CI	Obs	SIR	95% CI	Obs	SIR	95% CI
<45 years	4	50	13–128	2	275	33–992	—	0.0 ^a	0.0–660
45–59 years	5	12	4.0–29	12	19	10–34	2	2.6	0.3–9.3
≥60 years	1	10	0.3–58	19	7.1	4.3–11	13	2.7	1.5–4.7

^aExpected number.**TABLE VI.** Observed (Obs) Numbers of Death Cases and the Standard Mortality Ratios (SMR) with the 95% Confidence Intervals (95% CI) for the Men in 1967–1994, by Cohort

Cause of death	Asbestos sprayers			Asbestosis patients			Silicosis patients		
	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
All causes	34	2.8	1.9–3.8	67	1.9	1.5–2.5	82	1.4	1.1–1.8
Neoplasms	17	9.3	5.4–15	33	4.0	2.7–5.6	18	1.3	0.8–2.0
Lung cancer	8	17	7.2–33	25	8.0	5.2–12	10	1.9	0.9–3.5
Diseases of the circulatory system	3	0.7	0.2–2.1	14	0.8	0.4–1.3	30	1.0	0.7–1.4
Diseases of the respiratory system	4	12	3.3–31	14	5.9	3.2–10	22	5.4	3.4–8.2
Accidents, poisonings, and violence	6	1.3	0.5–2.9	4	1.5	0.4–3.9	5	1.3	0.4–3.1

patients in the cohorts. The observed numbers of cancers (all sites) among the women were 0, 4, and 1; the expected numbers were 0.2, 1.2, and 0.8, respectively. There were two cases of lung cancer (SIR 33, 95% CI 4.0–118) among the women with asbestosis.

Mortality

Among the men of both the asbestos sprayer and the asbestosis patient groups, the SMR for all causes, all cancers, lung cancer, and diseases of the respiratory system were significantly high (Table VI). All deaths attributed to respiratory problems were caused by asbestosis. Among the

silicosis patients only the SMR for diseases of the respiratory system was significantly high. Out of the 22 deaths related to respiratory problems, 17 were due to silicosis.

There were only eight deaths among the women. An elevated mortality (two deaths, SMR 14, 95% CI 1.7–52) for diseases of the respiratory system was noted for the female asbestosis patients.

DISCUSSION

We studied all the identified Finnish asbestos sprayers, a group of asbestosis patients, and a group of silicosis patients. The possible later diagnosis of cancer did not affect the

likelihood of being included in the cohort. The identification of the final cohort members, and follow-up for deaths and emigration through the population register, were complete for the period of this study, 1967–1993. The cancer registration system is virtually complete in Finland [Teppo et al., 1994], and the computerized record linkage procedures are accurate [Pukkala, 1992]. Cancers were not diagnosed at the Finnish Institute of Occupational Health (FIOH) during health examinations; instead, the diagnoses were taken from the Finnish Cancer Registry. If a suspicion of cancer arose during the periodic health examination (as it rarely did), the patient was sent to another hospital for further examination and treatment. If a cancer was diagnosed (a diagnosis is usually based on histological examination), the other hospital reported the new cancer to the Finnish Cancer Registry. Therefore we think that the possible bias of early detection of lung cancer is minimal.

Among the male asbestos sprayers and asbestosis patients, the excess of mesothelioma and lung cancer was high and significant; among the sprayers, an excess of other cancers was also noted. These were cancers of the stomach, rectum, and liver (one of each), a non-melanoma skin cancer, a meningioma, an acute lymphatic leucemia, and an intraperitoneal non-Hodgkin's lymphoma. The number of cases was small but most of them were intraperitoneal malignancies. This may reflect an asbestos-associated risk of these intraperitoneal cancers or misdiagnosed peritoneal mesotheliomas. Although the number of women was extremely small, a statistically significant excess of lung cancer was noted for the female asbestosis patients. An excess of cancer cases was obvious also when the group was compared with people of the same occupational branch and the same social status. In a study based on record linkage between the Finnish Cancer Registry and the population census of 1970, an SIR for all cancers among 35- to 64-year-old men in industrial and construction work was 1.1, and for lung cancer the corresponding value was 1.3 [Pukkala, 1995]. The cancer incidence was highest for the asbestos sprayers, obviously due to the high carcinogenic potency of crocidolite, which was the main type of asbestos sprayed in Finland. The exposure levels during spraying were also high. It has been estimated that exposure resulting from one to two days of asbestos spraying corresponds to that from one to four months of pipe insulation work (i.e., a pulmonary concentration of 1 million fibers per gram of dry tissue) [Tossavainen et al., 1994]. The SIR values for lung cancer among the sprayers (SIR 17) and the asbestosis patients (SIR 10) in our cohorts were higher than those found among anthophyllite miners (SIR 2.8) in an earlier study [Meurman et al., 1994]. The SMR values observed in earlier studies among insulators (4.4) [Selikoff and Seidman, 1991], asbestos textile workers (2.2) [Dement and Brown, 1994], chrysotile miners and millers (1.4) [Liddell, 1994],

and asbestos-exposed workers (1.4) [Rösler et al., 1994] have also been lower.

Our silicosis patients had a significantly increased incidence for all cancers (SIR 1.5), and specifically for lung cancer (SIR 2.7). For Chinese silicotic granite workers, the lung cancer incidence was at the same level, SIR 2.0, as in our study [Chia et al., 1991], as it was also in a register study of silicotics in Finland, SIR 2.9 [Partanen et al., 1994]. In mortality studies, high SMR values of 1.3 [Carta et al., 1991], 1.4 [Koskela et al., 1994], 2.0 [Ng et al., 1990], and 2.6 [Amandus et al., 1995] have been reported for lung cancer. Elevated mortality rates from all causes, and specifically for chronic lung diseases and tuberculosis, have been detected [Carta et al., 1991; Amandus et al., 1995; Goldsmith et al., 1995].

The interaction of lung cancer with exposure and smoking is important. There were no lung cancer cases among the nonsmokers. The smoking patterns of the cohorts in this study were similar to each other, and therefore the obtained relative risk differences were probably not due to differences in smoking habits. In addition, the prevalence of smoking was similar for the cohorts and the Finnish general population; for example, in 1979, 37% of Finnish men (43% of blue-collar workers) and 20% of Finnish women (23% of blue-collar workers) were regular smokers.

Of the lung cancers found in both the asbestos sprayers and the asbestosis patients, the SIR was highest for adenocarcinoma; this was followed by small cell carcinoma and squamous cell carcinoma. Adenocarcinoma also showed the highest relative risk of histological subtypes of lung cancer among Finnish pipe insulators [Pukkala, 1995]. Two-thirds of the lung cancers in our cohorts were situated in the lower lobes, whereas in average patients only one-third of lung cancers are located in this area. A similar trend was recently observed for surgically treated lung cancer patients who had been exposed to asbestos [Karjalainen et al., 1993].

The SIR and SMR values for all cancers and lung cancer were very similar. This finding indicates that, for fatal diseases, both incidence and mortality are reliable and interchangeable indicators of the frequency of occupational cancer.

The high incidence of lung cancer and mesothelioma among the asbestos sprayers indicates that other shipyard and construction-site workers with short-term indirect exposure during asbestos spraying may also have an increased risk of cancer. In addition, occupational lung cancer and mesothelioma among asbestos-exposed workers are not only diseases of the elderly, since the relative risk is high for middle-aged persons as well.

REFERENCES

- Amandus HE, Shy C, Castellan RM, Blair A, Heineman EF (1995): Silicosis and lung cancer among workers in North Carolina dusty trades. *Scand J Work Environ Health* 21 (suppl 2):81–83.
- Carta P, Cocco PL, Casula D (1991): Mortality from lung cancer among Sardinian patients with silicosis. *Br J Ind Med* 48:122–129.

- Chia S-E, Chia K-S, Phoon W-H, Lee H-P (1991): Silicosis and lung cancer among Chinese granite workers. *Scand J Work Environ Health* 17:170-174.
- Dement JM, Brown DP (1994): Lung cancer mortality among asbestos textile workers: A review and update. *Ann Occup Hyg* 38:525-532.
- Goldsmith DF, Beaumont JJ, Morrin LA, Schenker MB (1995): Respiratory cancer and other chronic disease mortality among silicotics in California. *Am J Ind Med* 28:459-467.
- IARC (International Agency for Research on Cancer) (1987): 'Asbestos.' IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, vol 14." Lyon, France: IARC.
- Karjalainen A, Anttila S, Heikkilä L, Kyyrönen P, Vainio H (1993): Lobe of origin of lung cancer among asbestos-exposed patients with and without diffuse interstitial fibrosis. *Scand J Work Environ Health* 19:102-107.
- Koskela R-S, Klockars M, Laurent H, Holopainen M (1994): Silica dust exposure and lung cancer. *Scand J Work Environ Health* 20:412-421.
- Liddell D (1994): Cancer mortality in chrysotile mining and milling: Exposure-response. *Ann Occup Hyg* 38:519-523.
- Meurman LO, Pukkala E, Hakama M (1994): Incidence of cancer among anthophyllite asbestos miners in Finland. *Occup Environ Med* 51:421-425.
- Ng TP, Chan SL, Lee J (1990): Mortality of a cohort of men in a silicosis register: Further evidence of an association with lung cancer. *Am J Ind Med* 17:163-171.
- Partanen T, Pukkala E, Vainio H, Kurppa K, Koskinen H (1994): Increased incidence of lung and skin cancer in Finnish silicotic patients. *J Occup Med* 36:616-622.
- Partanen T, Jaakkola J, Tossavainen A (1995): Silica, silicosis and cancer in Finland. *Scand J Work Environ Health* 21 (suppl 2):84-86.
- Pukkala E (1992): Use of record linkage in small-area studies. In Elliot P, Guzik J, English D, Stern R (eds): 'Geographical and Environmental Epidemiology.' Oxford: Oxford University Press, pp 125-131.
- Pukkala E (1995): Cancer risk by social class and occupation. A survey based on 109,000 cancer cases among working-aged Finns. In 'Contributions to Epidemiology and Biostatistics,' vol 7. Basel: Karger.
- Rösler JA, Weitowitz H-J, Rödelberger K (1994): Tumorrisiken durch Asbest in Deutschland im internationalen Vergleich. *Arbeitsmed Sozialmed Umweltmed* 29:458-463.
- Selikoff JJ, Seidman H (1991): Asbestos associated deaths among insulation workers in the United States and Canada 1967-1987. *Ann NY Acad Sci* 643:1-14.
- Smith AH, Lopipero PA, Barroga VR (1995): Meta-analysis of studies of lung cancer among silicotics. *Epidemiology* 6:617-624.
- Stayner LT, Dankovic DA, Lemen RA (1996): Occupational exposure to chrysotile asbestos and cancer risk: A review of the amphibole hypothesis. *Am J Public Health* 86:179-185.
- Steenland K, Loomis D, Shy C, Simonsen N (1996): Review of occupational lung carcinogens. *Am J Ind Med* 29:474-490.
- Teppo L, Pukkala E, Lehtonen M (1994): Data quality and quality control of population-based cancer registry. Experience in Finland. *Acta Oncol* 33:363-369.
- Tossavainen A, Karjalainen A, Karhunen PJ (1994): Retention of asbestos fibers on the human body. *Environ Health Perspect* 102:253-255.